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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,467	02/14/2006	Mark Louis Heiman	X16339	7932

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EXAMINER	
XIE, XIAOZHEN	

ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
07/03/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

Office Action Summary	Application No.	Applicant(s)	
	10/568,467	HEIMAN ET AL.	
	Examiner	Art Unit	
	Xiaozhen Xie	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-44 and 46-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *41-44,46 and 47* is/are allowed.

6)☒ Claim(s) *48-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *MeSH definitions*.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

Applicant's amendments of the specification and the claims filed 13 April 2007 have been entered.

In the previous office action (26 January 2007), it is indicated that claims 41-44 and 46-51 are allowable. However, upon further review, it has been found that claims 48-51 are subject to new grounds of rejections. Claims 1-40 and 45 are cancelled. Claims 41-44 and 46-51 are pending.

Specification

The objection to the specification for failing to include updated cross-reference to related applications is withdrawn in response to Applicant's amendment of the specification.

Claim Objections/Rejections Withdrawn

The rejection of claim 45 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in response to Applicant's cancellation of the claim.

The rejection of claim 45 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is withdrawn in response to Applicant's cancellation of the claim.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 48-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, *while being enabling for a method of treating obesity comprising administering a chimeric monoclonal antibody against Ghrelin or antigen-binding portion thereof, wherein the anti-Ghrelin antibody or antigen-binding portion thereof, comprises a light chain variable region comprising a peptide with the sequence shown in SEQ ID NO: 3, 4, 30 or 31, and a heavy chain variable region comprising a peptide with the sequence shown in SEQ ID NO: 12, 13, 32 or 33,* does not reasonably provide enablement for treating other disorders, such as NIDDM, Prader-Willi syndrome, an eating disorder, hyperphagia, impaired satiety, anxiety, and a gastric motility disorder. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims, the nature of the

invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986).

The claims recite treating obesity or a related disorder, wherein the related disorders include NIDDM, Prader-Willi syndrome, an eating disorder, hyperphagia, impaired satiety, anxiety, and a gastric motility disorder. The specification discloses that the ghrelin hormone, when acylated, binds the growth hormone secretagogue receptor (GHS-R1a) in the pituitary resulting in release of growth hormone; and the acylated form of ghrelin leads to fat deposition when administered to mice. The specification discloses that Ghrelin serum levels increase during food deprivation in animals, peak prior to eating, and decrease upon refeeding. The specification discloses that persons with Prader-Willi syndrome, a genetic disorder that causes severe obesity with uncontrollable appetite, have extremely high levels of ghrelin. The specification discloses that ghrelin plays a key role in motivating feeding. The specification discloses that monoclonal anti-ghrelin antibodies, which preferentially bind acylated human ghrelin with respect to unacylated human ghrelin, are useful for treatment of obesity. The prior art also teaches the use of anti-ghrelin antibodies for the treatment of obesity with a decrease in both food intake and body weight in murine models (WO 01/87335, IDS item BB; Murakami et al., J. Endocrinology 174:283-288, 2002, IDS item CG; Nakazato et al., Nature, 2001, Vol. 409:194-198, references provided previously). The

specification, however, has not provided sufficient teachings for treating other disorders, including NIDDM, Prader-Willi syndrome, an eating disorder, hyperphagia, impaired satiety, anxiety, and a gastric motility disorder. These diseases differ in pathology and treatment. Controlling body weight gain may not be sufficient to treat the diseases. Further, some subjects with the disorders do not necessarily develop obesity. For example, an eating disorder can be *anorexia nervosa* or *Bulimia nervosa*, in which patients weigh at least 15% below what is normal for others of the same height and age, and patients frequently have other mental disorders such as depression, substance abuse, and anxiety disorders (see National Mental Health Information Center webpages, attached). Hiraiwa et al. (Brain dev., 2007, Feb. 19, epub) teach that Prader-Willi syndrome (PWS) is a genetically determined neurodevelopmental disorder characterized by mental retardation and distinct physical, behavioral, and psychiatric features; young adults with PWS have significantly higher rates of behavioral and psychiatric disorders than individuals with intellectual disability disorders without PWS, such as stubbornness, hyperphagia, temper tantrums, self-injurious behavior, hypersomnia, inactivity, and delusion; and degree of obesity was not necessarily related to behavioral and psychiatric features associated with PWS (see abstract). A gastric motility disorder affects the motor function of the esophageal sphincter or the esophagus body, and the failure of the sphincters to maintain a tonic pressure may result in gastric reflux of food and acid into the esophagus (see MESH definition). Anxiety disorders are metal disorders that can be agoraphobia, neurocirculatory asthenia, obsessive-compulsive disorder, panic disorder, phobic disorders, and stress

disorders (see MESH definition), and many of the individuals with such disorders do not develop obesity.

The claims encompass treating disorders with many causes, striking many tissues, and with many different outcomes. Some disorders exhibit more diversity, e.g., some patients develop weight gain and some patients exhibit weight loss. The specification fails to provide guidance as to how the artisan could treat all these diseases. Thus, the scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure set forth in the specification.

Due to the large quantity of experimentation necessary to determine whether the anti-Ghrelin antibody or antigen-binding portion thereof can be used to treat disorders such as recited in claim 49, the lack of direction/guidance presented in the specification, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the diversity, complexity and unpredictability of the diseases from different tissue origin, the breadth of the claims, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

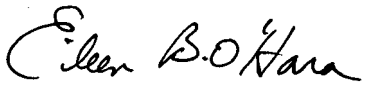
CLAIMS 41-44, 46 AND 47 ARE ALLOWABLE.

CLAIMS 48-51 ARE REJECTED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie, Ph.D whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph. D. can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



EILEEN B. O'HARA
PRIMARY EXAMINER

Xiaozhen Xie, Ph. D.
June 18, 2007